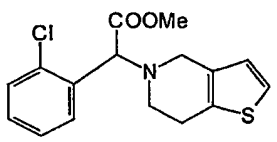
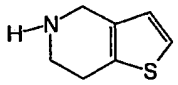
We claim,

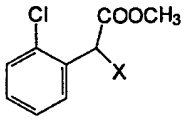
1. An industrial process for manufacture of Clopidogrel of Formula I starting from 2-(2-thienyl)ethylamine characterized in that the said process comprising



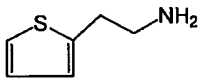
Formula I



Formula II



X = Cl or Br
Formula III



Formula IV

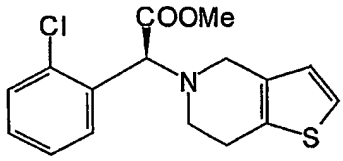
   i) a one-pot conversion of 2-(2-thieno)ethylamine (IV) by the action of paraformaldehyde and an acid catalyst in a single vessel without isolation of 2-(2-thienyl)ethyl formimine intermediate into 4,5,6,7-tetrahydrothieno(3,2-c)pyridine intermediate of formula II, and

   ii) reacting the said intermediate with halo benzene derivative of Formula III in presence of a base in solvent selected from dichloroethane or water or a mixture of water and hydrocarbon/chlorinated hydrocarbon solvents at a temperature ranging from 20 to 90 °C to obtain clopidogrel and isolating said clopidogrel as free base or hydrogen sulphate salt.

2. The process as claimed in claim 1, wherein the acid catalyst is a mineral acid such as hydrochloric acid.
3. The process as claimed in claim 1 or 2, wherein the one-pot reaction of 2-(2-thienyl) ethylamine with paraformaldehyde and hydrochloric acid is performed in hydrocarbon solvents selected from aliphatic, aromatic hydrocarbons and chlorinated hydrocarbons, preferably dichloroethane.

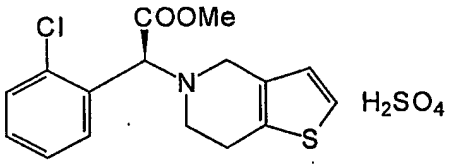
4. The process as claimed in any one of the preceding claim, wherein 2-(2-thienyl)ethyl formimine is formed in-situ by effective removal of water at reflux temperature and cyclized in presence of anhydrous hydrochloric acid.
5. The process as claimed in any one of the preceding claim, wherein the one-pot acid catalyzed cyclization of the intermediate 2-(2-thienyl)ethyl formimine is carried out at a temperature ranging from about 60°C to 90°C.
6. The process as claimed in claim 1, wherein reaction of 4,5,6,7-tetrahydrothieno(3,2-c)pyridine of formula II with halobenzene derivative of Formula III is carried out in dichloroethane.
7. The process as claimed in claim 6, wherein the base is selected from trialkyl amines, preferably triethylamine.
8. The process as claimed in claim 7, wherein reaction is performed at a temperature of 50°C to 80°C.
9. A process for preparation of clopidogrel of Formula I comprising reaction of 4,5,6,7-tetrahydrothieno(3,2-C)pyridine hydrochloride of formula II with halobenzene derivative of Formula III in presence of a base characterized in water or in a mixture of water and hydrocarbon solvents selected from aliphatic, aromatic and chlorinated hydrocarbons.
10. The process as claimed in claim 9, wherein the base is sodium carbonate or potassium carbonate.
11. The process as claimed in claim 10, wherein reaction is performed at a temperature of 20°C to 40°C.
12. The process as claimed in claim 1 wherein, the Clopidogrel hydrogen sulphate is prepared in a one-pot procedure without isolation of intermediates comprising an acid catalyzed cyclization of 2-(2-thienyl)ethylamine with paraformaldehyde to form 4,5,6,7-tetrahydrothieno(3,2-c)pyridine of Formula II as hydrochloride, reacting the said compound of Formula II *in-situ* with a compound of Formula III in presence of base, and isolating Clopidogrel as hydrogen sulphate salt.
13. The process as claimed in claim 12, wherein the base is sodium carbonate or potassium carbonate.

14. The process as claimed in any one of the preceding claim, wherein the halo derivative of Formula III is methyl-1-bromo-(2-chlorophenyl)acetate.
15. The process as claimed in claim 1, further comprising resolution of racemic Clopidogrel using anhydrous levo-rotatory camphor sulphonic acid in a solvent system selected from a combination of polar and apolar/weakly polar solvents to obtain dextrorotatory clopidogrel of Formula IA.



Formula IA

16. The process as claimed in claim 15, wherein the combination solvents are acetone:dichloromethane, acetone: toluene, or acetone: cyclohexane
17. The process as claimed in claim 16, wherein the proportion of acetone and dichloromethane is 10: 1.0
18. An industrial process for manufacture of Form I crystals of (+)-(S)-clopidogrel hydrogen sulphate of Formula IB comprising:



Formula IB

dissolving methyl (+)-(S)-α-(2-chlorophenyl)-4,5,6,7-tetrahydrothieno[3,2-C]pyridine-5-acetate [i.e., (+)-(S)-clopidogrel base] in methyl propyl ketone, methyl isopropyl ketone, diethyl ketone or their mixture thereof, mixture of ethyl acetate and methyl propyl ketone, mixture of ethyl acetate and methyl isopropyl ketone, or mixture of ethyl acetate and diethyl ketone; cooling said clopidogrel base solution to a temperature of about -10 to 20 °C; adding concentrated sulphuric acid to said cooled solution; maintaining said salt mixture at a temperature in the range of about 10 ° to 30 ° C to effect precipitation of (+)-(S)-clopidogrel hydrogen sulphate in Form I and filtering said crystals of Form I.

19. The process as claimed in claims 18 , wherein said mixture of ketone solvents comprises mixture of methyl propyl ketone and methyl isopropyl ketone, mixture of methyl propyl ketone and diethyl ketone, mixture of methyl isopropyl ketone and diethyl ketone, in all proportion.
20. The process as claimed in claim 19, wherein the addition of said concentrated sulphuric acid is carried out while maintaining the temperature at –10 to 10° C.
21. A process for the manufacture of Form I crystals of (+)-(S)-clopidogrel hydrogen sulphate of Formula I, wherein the said process comprising: dissolving methyl (+)-(S)-α-(2-chlorophenyl)-4,5,6,7-tetrahydrothieno[3,2-C]pyridine-5-acetate [(+)-(S)-clopidogrel base] in ethyl acetate; cooling to a temperature of 18° to 20° C; mixing with concentrated sulphuric acid with or without allowing the temperature to raise to 28° to 30°C; maintaining the salt mixture at 28° to 30° C for 7 to 10 hours to effect precipitation of (+)-(S)-clopidogrel hydrogen sulphate in Form I and filtering said crystals of Form I.
22. The process as claimed in claim 21, wherein the addition of said concentrated sulphuric acid is carried out while maintaining the temperature at 18 to 24° C.
23. The process as claimed in any one of the preceding claim, wherein the strength of said sulphuric acid is about 95 to 98 % concentrated sulphuric acid.
24. The process as claimed in any one of the preceding claim, wherein the molar ratio of sulphuric acid used is 1.02 to1.1 relative to (+)-(S)-clopidogrel base.
25. An industrial process for the preparation of Form II of (+)-(S)-clopidogrel hydrogen sulphate from solvents selected from ethyl acetate, isopropyl alcohol and tetrahydrofuran under conditions effective to form Form II.
26. The process as claimed in claim 25, wherein Form II of (+)-(S)-clopidogrel hydrogen sulphate is prepared from ethyl acetate comprising the steps of, dissolving (+)-(S)-clopidogrel base of Formula I in ethyl acetate; cooling the mixture to 5° to 10° C; mixing concentrated sulphuric acid while maintaining the said temperature; and maintaining the mixture under stirring at a temperature of 10° to 15° C for a period of 8 to 12 hours.
27. The process as claimed in claim 25, wherein Form II of (+)-(S)-clopidogrel hydrogen sulphate is prepared from ethyl acetate comprising the steps of,

dissolving (+)-(S)-clopidogrel base of Formula I in ethyl acetate at a temperature of 45° to 50°C; mixing concentrated sulphuric acid while maintaining the said temperature; maintaining the mixture under stirring for a period of 1 to 3 hours at 45° to 50° C; cooling to a temperature of 30° to 32°C in 1 hour and maintaining for a period of 3 to 4 hours to yield (+)-(S)-clopidogrel hydrogen sulphate Form II.

28. The process as claimed in claim 25, wherein Form II of (+)(S)clopidogrel hydrogen sulphate is prepared from tetrahydrofuran comprising the steps of , dissolving (+)-(S)-clopidogrel base of Formula I in tetrahydrofuran at a temperature of 25° to 30°C; cooling to a temperature of 10° to 15° C; mixing concentrated sulphuric acid while maintaining the said temperature; and maintaining for a period of 6 to 8 hours to yield (+)-(S)-clopidogrel hydrogen sulphate Form II.
29. The process as claimed in claim 25, wherein Form II of (+)-(S)-clopidogrel hydrogen sulphate is prepared from isopropyl alcohol comprising the steps of, dissolving (+)-(S)-clopidogrel base of Formula I in isopropyl alcohol at a temperature of 28° to 30°C; mixing with concentrated sulphuric acid while maintaining the said temperature; and maintaining the mixture for a period of 6 to 8 hours at 28 ° to 30° C to yield (+)-(S)-clopidogrel hydrogen sulphate Form II.
30. Clopidogrel hydrogen sulphate prepared substantially according to any one of the preceding claims.
31. A process for clopidogrel hydrogen sulphate and its polymorphs as substantially described herein with reference to the examples 1 to 15.